REMARKS

Claims 1-19 were pending in this application. Claims 1-5 have been canceled. Claims 6, 10, and 14 have been amended. New claims 20-21 have been presented. Support for the amendments to the specification on page 52, line 3, and lines 1-2, and page 54, lines 1-2, can be found in the specification, for example in claim 7, page 83, lines 27-28. Upon entry of the present amendment, Claims 5-21 would be pending in this application.

I. Rejection Under 35 U.S.C. § 102 (b)

The Office has maintained the rejection of claims 1-2 and 4 under 35 U.S.C § 102(b) as being anticipated by Mynott et al. The Office alleges that Mynott et al. teaches that bromelain, a MEK inhibitor, is useful in a method of treating rheumatoid arthritis.

Applicants have canceled claims 1-5. Accordingly, Applicants respectfully request that this rejection be withdrawn.

II. Rejection under 35 U.S.C § 103

The Office has maintained the rejection of Claims 1-19 under 35 U.S.C. § 103(a) as allegedly being obvious over Miyazawa et al., Jackson et al., Henry et al., and McGilvray in view of Bridges.

Applicants respectfully disagree with the Examiner's contentions and maintain that the claims, as amended, are not obvious under 35 U.S.C. § 103(a) over Miyazawa et al., Jackson et al., Henry et al., and McGilvray in view of Bridges. As set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the prior art references (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in the Applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)." As the Federal Circuit has also stated, "[a] general incentive does not make obvious a particular result, nor does the existence

of techniques by which those efforts can be carried out." *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

Applicants respectfully point out that Miyazawa et al., Jackson et al., and Henry et al. disclose inhibitors of a particular MAP kinase - p38 MAP kinase. The compounds used in the present methods of the claimed invention, application, however, are not p38 MAP kinase inhibitors. Rather, they are MEK1 and MEK2 inhibitors, which are MAP kinase kinase inhibitors.

The MEK1/MEK2 inhibitors used in the presently claimed methods act on a different pathway that p38 kinase inhibitors of Miyazawa et al., Jackson et al., and Henry et al. Furthermore, the activation of p38 MAP kinase and the c-jun N-terminal kinases (JNKs), "rel(y) on their phosphorylation at specific dual phosphorylation motifs, namely the sequences Thr-Pro-Tyr (TPY) for JNK and Thr-Glu-Tyr (TGY) for p38 MAP kinase, respectively.... These residues are specifically phosphorylated by MKK/MEK homologues distinct from MKK/MEKs 1 and 2, that are responsible for the activation of the classical p42/44 MAP kinase isoforms." (page 404 of A. Paul, et al.,"Stress-activated Protein Kinases: Activation, Regulation and Function", Cellular Signaling, Vol. 9, No. 6, 403-410, (1997)).

In fact, it has been shown that a MEK inhibitor used in the methods of the claimed invention (see e.g., claims 14-17, and 20 and 21), 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, does not inhibit the phosphorylation of Jun kinase or p38 kinase in a cellular assay and does not substantially inhibit MKK3, an activator of p38 kinase, in an in vitro kinase assay. (See pages 810-811 of Sebolt-Leopold et al.,"Blockade of the MAP kinase pathway suppresses growth of colon tumors in vivo", *Nature Medicine*, Vol. 5, No. 7, 810-816 (1999)). Given that the MEK inhibitors used in the present invention do not substantially inhibit p38 or MKK3, one of skill in the art would not have been motivated to combine the teachings of Miyazawa et al., Jackson et al., and Henry et al., which disclose p38 inhibitors, with McGilavray and Bridges to arrive at the present invention. Accordingly, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-622-2095.

Respectfully submitted,

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